

WHAT IS CLAIMED IS:

1 1. A unit dosage form as an adjunct to biguanide or sulfonylurea therapy
2 for supporting mitochondrial metabolism as a method for the prevention, management and
3 clinical amelioration of insulin resistance and type 2 diabetes and conditions giving rise
4 thereto, said unit dosage form comprising as active ingredients:

- 5 (a) L-carnitine,
- 6 (b) ascorbic acid,
- 7 (c) choline,
- 8 (e) taurine,
- 9 (f) folic acid, and
- 10 (g) magnesium.

1 2. A unit dosage form in accordance with claim 1 in which said active
2 ingredients are formulated as a substantially homogeneous tablet or capsule that releases all
3 of said active ingredients into the stomach upon ingestion for contact with gastric fluid.

1 3. A unit dosage form in accordance with claim 2 in which:

- 2 (a) said L-carnitine is in an amount ranging from about 90 mg to about 2500
- 3 mg, and
- 4 (b) said ascorbic acid is in an amount ranging from about 75 mg to about
- 5 3000 mg,
- 6 (c) said choline is in an amount ranging from about 15 mg to about 250 mg,
- 7 (d) said taurine is in an amount ranging from about 75 mg to about 3000 mg,
- 8 (e) said magnesium is in an amount ranging from about 30 mg to about 1000
- 9 mg, and
- 10 (d) said folic acid is in an amount ranging from about 0.03 mg to about 2 mg.

1 4. A unit dosage form as an adjunct to biguanide or sulfonylurea therapy
2 for the preservation of plasma and mitochondrial membrane integrity for use as a method for
3 the prevention, management and clinical amelioration of insulin resistance and type 2
4 diabetes and conditions giving rise thereto, said unit dosage form comprising as active
5 ingredients:

- 6 (a) D, α -lipoic acid,
- 7 (b) N, acetyl-cysteine,

- 8 (c) ubiquinone,
- 9 (d) selenium,
- 10 (e) a member selected from the group consisting of D, α -tocopherol and
- 11 tocotrienol,
- 12 (f) L-arginine, and
- 13 (g) tetrahydrobiopterin.

1 5. A unit dosage form in accordance with claim 4 in which said active
2 ingredients are formulated as a substantially homogeneous tablet or capsule that releases all
3 of said active ingredients into the stomach upon ingestion for contact with gastric fluid.

1 6. A unit dosage form in accordance with claim 5 in which:

2 (a) said D, α -lipoic acid is in an amount ranging from about 30 mg to about
3 1500 mg,

4 (b) said N, acetyl-cysteine is in an amount ranging from about 75 mg to
5 about 3900 mg,

6 (c) said ubiquinone is in an amount ranging from about 4.5 mg to about 225
7 mg,

8 (d) said selenium is in an amount ranging from about 0.02 mg to about 0.75
9 mg,

10 (e) said D, α -tocopherol or tocotrienol is in an amount ranging from about 15
11 mg to about 1600 mg,

12 (f) said L-arginine is in an amount ranging from about 75 mg to about 3100
13 mg, and

14 (f) said tetrahydrobiopterin is in an amount ranging from about 24 mg to about
15 3000 mg.

1 7. A unit dosage form as an adjunct to biguanide or sulfonylurea therapy
2 specifically for nocturnal use as a method for the prevention, management and clinical
3 amelioration of insulin resistance and type 2 diabetes and conditions giving rise thereto, said
4 unit dosage form comprising as active ingredients:

- 5 (a) melatonin,
- 6 (b) L-carnitine,
- 7 (c) Ubiquinone,
- 8 (d) folic acid,

- 9 (e) magnesium, and
10 (f) L-arginine.

1 8. A unit dosage form in accordance with claim 7 in which said active
2 ingredients are formulated as a substantially homogeneous tablet or capsule that releases all
3 of said active ingredients into the stomach upon ingestion for contact with gastric fluid.

1 9. A unit dosage form in accordance with claim 8 in which:

2 (a) said melatonin is in an amount ranging from about 0.15 mg to about 7.5

3 mg,

4 (b) said L-carnitine is in an amount ranging from about 90 mg to about 2500

5 mg,

6 (c) said ubiquinone is in an amount ranging from about 4.5 mg to about 225

7 mg,

8 (d) said folic acid is in an amount ranging from about 0.03 mg to about 2 mg,

9 (e) said magnesium is in an amount ranging from about 30 mg to about 1000

10 mg, and

11 (f) said L-arginine is in an amount ranging from about 75 mg to about 3100

12 mg.

1 10. A unit dosage form for use as an adjunct to biguanide or sulfonylurea
2 therapy alternative to insulin for use as a method for the prevention, management and clinical
3 amelioration of insulin resistance and type 2 diabetes and conditions giving rise thereto, said
4 unit dosage form comprising as active ingredients:

5 (a) vanadium,

6 (b) L-arginine,

7 (c) chromium, and

8 (d) zinc.

1 11. A unit dosage form in accordance with claim 10 in which said active
2 ingredients are formulated as a substantially homogeneous tablet or capsule that releases all
3 of said active ingredients into the stomach upon ingestion for contact with gastric fluid.

1 12. A unit dosage form in accordance with claim 11 in which:

2 (a) said vanadium is in an amount ranging from about 7.5 mg to about 375

3 mg,

4 (b) said L-arginine is in an amount ranging from about 75 mg to about 3100
5 mg,

6 (c) said chromium is in an amount ranging from about 0.01 mg to about 0.63
7 mg, and

8 (d) said zinc is in an amount ranging from about 1.5 mg to about 100 mg.

1 13. A unit dosage form in accordance with claim 1 in which said unit
2 dosage form is a bilayer tablet comprising an immediate-release layer and a sustained-release
3 layer, said active ingredients are distributed between said immediate-release layer and said
4 sustained-release layer in the following approximate proportions expressed as relative weight
5 percents:

	<u>Immediate-Release Layer</u>	<u>Sustained-Release Layer</u>
6 L, carnitine	40-60%	balance
7 ascorbic acid	40-60%	balance
8 choline	100%	
9 folic acid	100%	
10 taurine	40-60%	balance
11 magnesium	40-60%	balance

1 14. A unit dosage form in accordance with claim 4 in which said unit
2 dosage form is a bilayer tablet comprising an immediate-release layer and a sustained-release
3 layer, said active ingredients are distributed between said immediate-release layer and said
4 sustained-release layer in the following approximate proportions expressed as relative weight
5 percents:

	<u>Immediate-Release Layer</u>	<u>Sustained-Release Layer</u>
6 D,α-lipoic acid	40-60%	balance
7 N-acetyl-cysteine	40-60%	balance
8 ubiquinone	40-60%	balance
9 selenium	40-60%	balance
10 tocotrienol	100%	
11 L-arginine	40%-60%	balance
12 tetrahydrobiopterin	40%-60%	balance

1 15. A unit dosage form in accordance with claim 7 in which said unit
2 dosage form is a bilayer tablet comprising an immediate-release layer and a sustained-release

layer, said active ingredients are distributed between said immediate-release layer and said sustained-release layer in the following approximate proportions expressed as relative weight percents:

	<u>Immediate-Release Layer</u>	<u>Sustained-Release Layer</u>
melatonin	40-60 %	balance
L-carnitine	40-60%	balance
zinc	40%-60%	balance
folic acid	100%	
magnesium	40-60%	balance
ubiquinone	100%	

16. A unit dosage form in accordance with claim 10 in which said unit dosage form is a bilayer tablet comprising an immediate-release layer and a sustained-release layer, said active ingredients are distributed between said immediate-release layer and said sustained-release layer in the following approximate proportions expressed as relative weight percents:

	<u>Immediate-Release Layer</u>	<u>Sustained-Release Layer</u>
vanadium	40-60 %	balance
L-arginine	40-60%	balance
chromium	40%-60%	balance
zinc	40%-60%	balance

17. A unit dosage form in accordance with claim 4 in which said α -lipoic acid is in the form of a member selected from the group consisting of an α -lipoic acid salt of a metal ion selected from the group consisting of Mg^{2+} and Zn^{2+} , and a complex of α -lipoic acid, a metal ion selected from the group consisting of Mg^{2+} and Zn^{2+} , and an anion selected from the group consisting of hydroxide, halide, acetate, and ascorbate.

18. A unit dosage form in accordance with claims 4, 7 or 10 in which said L-arginine is in the form of a member selected from the group consisting of L-arginine ascorbate, bis-L-arginine ascorbate, L-arginine salt of a metal ion selected from the group consisting of Mg^{2+} and Zn^{2+} , bis-L-arginine salt of a metal ion selected from the group consisting of Mg^{2+} and Zn^{2+} , and a complex of L-arginine or bis-L-arginine, a metal ion selected from the group consisting of Mg^{2+} and Zn^{2+} , and an anion selected from the group consisting of hydroxide, halide, acetate, and ascorbate.

1 19. A unit dosage form in accordance with claims 1 or 7 in which said
2 L-carnitine is in the form of a member selected from the group consisting of L-carnitine
3 ascorbate, bis-L-carnitine ascorbate, L-carnitine salt of a metal ion selected from the group
4 consisting of Mg^{2+} and Zn^{2+} , bis-L-carnitine salt of a metal ion selected from the group
5 consisting of Mg^{2+} and Zn^{2+} , and a complex of L-carnitine or bis-L-carnitine, a metal ion
6 selected from the group consisting of Mg^{2+} and Zn^{2+} , and an anion selected from the group
7 consisting of hydroxide, halide, acetate, and ascorbate.

1 20. A unit dosage form in accordance with claim 1 in which said L-
2 taurine is in the form of a member selected from the group consisting of L-aurine ascorbate,
3 bis-L-aurine ascorbate, L-aurine salt of a metal ion selected from the group consisting of
4 Mg^{2+} and Zn^{2+} , bis-L-aurine salt of a metal ion selected from the group consisting of Mg^{2+}
5 and Zn^{2+} , and a complex of L-aurine or bis-L-aurine, a metal ion selected from the group
6 consisting of Mg^{2+} and Zn^{2+} , and an anion selected from the group consisting of hydroxide,
7 halide, acetate, and ascorbate.

1 21. A unit dosage form in accordance with claims 1 or 7 in which said
2 magnesium is in the form of a member selected from the group consisting of magnesium,
3 magnesium L-arginate, magnesium L-arginine ascorbate and bis-ascorbate, magnesium α -
4 lipoate, magnesium α -lipoate ascorbate and bis-ascorbate, magnesium taurate, magnesium
5 taurine ascorbate and bis-ascorbate, magnesium L-acetylcysteine, magnesium L-carnitate,
6 magnesium L-carnitine ascorbate and bis-ascorbate, magnesium ascorbate and magnesium
7 bis-ascorbate.

1 22. A unit dosage form in accordance with claim 10 in which said zinc is
2 in the form of a member selected from the group consisting of zinc halide, zinc sulfate, zinc
3 L-carnitate, zinc L-carnitate ascorbate and bis-ascorbate, zinc taurate, zinc taurine ascorbate
4 and bis-ascorbate, zinc L-arginate, zinc L-arginine ascorbate and bis-ascorbate, zinc L-
5 carnitate, zinc L-carnitine ascorbate and bis-ascorbate, zinc phosphate, zinc acetate, zinc
6 ascorbate, and zinc bis-ascorbate.

1 23. A unit dosage form in accordance with claim 10 in which said
2 vanadium is in the form of a member selected from the group consisting of vanadate,
3 peroxovanadate, vanadyl sulfate salts, and bis(maltolato)oxovanadium(IV).

1 24. A unit dosage form in accordance with claims 4 or 6 in which said
2 D, α -tocopherol is present in the form of a member selected from the group consisting of
3 D, α -tocopherol succinate, D, α -tocopherol nicotinate, D, α -tocopherol picolinate,
4 D, α -tocopherol acetate, and tocotrienol.

1 25. A unit dosage form in accordance with claims 14 or 24 in which said
2 tocotrienol is present in the form of a member selected from the group consisting of
3 tocotrienol succinate, tocotrienol nicotinate, tocotrienol picolinate, and tocotrienol acetate.

1 26. A unit dosage form in accordance with claim 10 in which said
2 chromium is in the form of a member selected from the group consisting of chromium
3 dinicotinate, and chromium tripicolinate.

1 27. A method for treating a patient who is undergoing biguanide therapy
2 for the prevention, management, and clinical amelioration of insulin resistance and type 2
3 diabetes and conditions giving rise thereto, to reduce undesirable physiological side effects,
4 and enhance the therapeutic effectiveness, of said biguanide therapy, said method comprising
5 administering to said patient a unit dosage form comprising as active ingredients:

- 6 (a) L-carnitine,
- 7 (b) ascorbic acid,
- 8 (c) choline,
- 9 (e) taurine,
- 10 (f) folic acid, and
- 11 (g) magnesium.

1 28. A method in accordance with claim 27 in which said active ingredients
2 are formulated as a substantially homogeneous tablet or capsule that releases all of said active
3 ingredients into the stomach upon ingestion for contact with gastric fluid.

- 1 29. A method in accordance with claim 28 in which:
- 2 (a) said L-carnitine is in an amount ranging from about 90 mg to about 2500
 - 3 mg, and
 - 4 (b) said ascorbic acid is in an amount ranging from about 75 mg to about
 - 5 3000 mg,
 - 6 (c) said choline is in an amount ranging from about 15 mg to about 250 mg,

(d) said taurine is in an amount ranging from about 75 mg to about 3000 mg,
(e) said magnesium is in an amount ranging from about 30 mg to about 1000
mg, and

(d) said folic acid is in an amount ranging from about 0.03 mg to about 2 mg.

30. A method for treating a patient who is undergoing biguanide therapy for the preservation of plasma and mitochondrial membrane integrity for the prevention, management, and clinical amelioration of insulin resistance and type 2 diabetes and conditions giving rise thereto, to reduce undesirable physiological side effects, and enhance the therapeutic effectiveness, of said biguanide therapy, said method comprising administering to said patient a unit dosage form comprising as active ingredients:

- (a) D, α -lipoic acid,
- (b) N, acetyl-cysteine,
- (c) ubiquinone,
- (d) selenium,
- (e) a member selected from the group consisting of D, α -tocopherol and tocotrienol,
- (f) L-arginine, and
- (g) tetrahydrobiopterin.

31. A method in accordance with claim 30 in which said active ingredients are formulated as a substantially homogeneous tablet or capsule that releases all of said active ingredients into the stomach upon ingestion for contact with gastric fluid.

32. A method in accordance with claim 34 in which:

- (a) said D, α -lipoic acid is in an amount ranging from about 30 mg to about 1500 mg,
- (b) said N, acetyl-cysteine is in an amount ranging from about 75 mg to about 3900 mg,
- (c) said ubiquinone is in an amount ranging from about 4.5 mg to about 225 mg,
- (d) said selenium is in an amount ranging from about 0.02 mg to about 0.75 mg,
- (e) said D, α -tocopherol or tocotrienol is in an amount ranging from about 15 mg to about 1600 mg,

12 (f) said L-arginine is in an amount ranging from about 75 mg to about 3100
13 mg, and

14 (f) said tetrahydrobiopterin is in an amount ranging from about 24 mg to about
15 3000 mg.

1 33. A method for treating a patient who is undergoing nocturnal biguanide
2 therapy for the preservation of plasma and mitochondrial membrane integrity for the
3 prevention, management, and clinical amelioration of insulin resistance and type 2 diabetes
4 and conditions giving rise thereto, to reduce undesirable physiological side effects, and
5 enhance the therapeutic effectiveness, of said biguanide therapy, said method comprising
6 administering to said patient a unit dosage form comprising as active ingredients:

7 (a) melatonin,

8 (b) L-Carnitine,

9 (c) ubiquinone,

10 (d) folic acid,

11 (e) magnesium, and

12 (f) L-arginine.

1 34. A method in accordance with claim 33 in which said active ingredients
2 are formulated as a substantially homogeneous tablet or capsule that releases all of said active
3 ingredients into the stomach upon ingestion for contact with gastric fluid.

1 35. A method in accordance with claim 34 in which:

2 (a) said melatonin is in an amount ranging from about 0.15 mg to about 7.5
3 mg,

4 (b) said L-carnitine is in an amount ranging from about 90 mg to about 2500
5 mg,

6 (c) said ubiquinone is in an amount ranging from about 4.5 mg to about 225
7 mg,

8 (d) said folic acid is in an amount ranging from about 0.03 mg to about 2 mg,

9 (e) said magnesium is in an amount ranging from about 30 mg to about 1000
10 mg, and

11 (f) said L-arginine is in an amount ranging from about 75 mg to about 3100
12 mg.

1 **36.** A method for treating a patient who is undergoing biguanide therapy as
2 an alternative to insulin for the prevention, management, and clinical amelioration of insulin
3 resistance and type 2 diabetes and conditions giving rise thereto, to reduce undesirable
4 physiological side effects, and enhance the therapeutic effectiveness, of said biguanide
5 therapy, said method comprising administering to said patient a unit dosage form comprising
6 as active ingredients:

- 7 (a) vanadium,
8 (b) L-arginine,
9 (c) chromium, and
10 (d) zinc.

1 **37.** A method in accordance with claim 36 in which said active ingredients
2 are formulated as a substantially homogeneous tablet or capsule that releases all of said active
3 ingredients into the stomach upon ingestion for contact with gastric fluid.

1 **38.** A method in accordance with claim 37 in which:

- 2 (a) said vanadium is in an amount ranging from about 7.5 mg to about 375
3 mg,
4 (b) said L-arginine is in an amount ranging from about 75 mg to about 3100
5 mg,
6 (c) said chromium is in an amount ranging from about 0.01 mg to about 0.63
7 mg, and
8 (d) said zinc is in an amount ranging from about 1.5 mg to about 100 mg.

1 **39.** A method in accordance with claim 27 in which said unit dosage form
2 is a bilayer tablet comprising an immediate-release layer and a sustained-release layer, said
3 active ingredients are distributed between said immediate-release layer and said sustained-
4 release layer in the following approximate proportions expressed as relative weight percents:

	<u>Immediate-Release Layer</u>	<u>Sustained-Release Layer</u>
L, carnitine	40-60%	balance
ascorbic acid	40-60%	balance
choline	100%	
folic acid	100%	
taurine	40-60%	balance

11 magnesium 40-60% balance

1 **40.** A method in accordance with claim **30** in which said unit dosage form
2 is a bilayer tablet comprising an immediate-release layer and a sustained-release layer, said
3 active ingredients are distributed between said immediate-release layer and said sustained-
4 release layer in the following approximate proportions expressed as relative weight percents:

	<u>Immediate-Release Layer</u>	<u>Sustained-Release Layer</u>	
5			
6	D,α-lipoic acid	40-60%	balance
7	N-acetyl-Cysteine	40-60%	balance
8	ubiquinone	40-60%	balance
9	Selenium	40-60%	balance
10	tocotrienol	100%	
11	L-arginine	40%-60%	balance
12	tetrahydrobiopterin	40%-60%	balance

1 **41.** A method in accordance with claim **33** in which said unit dosage form
2 is a bilayer tablet comprising an immediate-release layer and a sustained-release layer, said
3 active ingredients are distributed between said immediate-release layer and said sustained-
4 release layer in the following approximate proportions expressed as relative weight percents:

	<u>Immediate-Release Layer</u>	<u>Sustained-Release Layer</u>	
5			
6	melatonin	40-60 %	balance
7	L-carnitine	40-60%	balance
8	zinc	40%-60%	balance
9	folic acid	100%	
10	magnesium	40-60%	balance
11	ubiquinone	100%	

1 **42.** A method in accordance with claim **36** in which said unit dosage form
2 is a bilayer tablet comprising an immediate-release layer and a sustained-release layer, said
3 active ingredients are distributed between said immediate-release layer and said sustained-
4 release layer in the following approximate proportions expressed as relative weight percents:

	<u>Immediate-Release Layer</u>	<u>Sustained-Release Layer</u>	
5			
6	vanadium	40-60 %	balance
7	L-arginine	40-60%	balance
8	chromium	40%-60%	balance

5 taurine ascorbate and bis-ascorbate, magnesium L-acetylcysteine, magnesium L-carnitate,
6 magnesium L-carnitine ascorbate and bis-ascorbate, magnesium ascorbate and magnesium
7 bis-ascorbate.

1 **48.** A method in accordance with claim **36** in which said zinc is in the form
2 of a member selected from the group consisting of zinc halide, zinc sulfate, zinc L-carnitate,
3 zinc L-carnitate ascorbate and bis-ascorbate, zinc taurate, zinc taurine ascorbate and bis-
4 ascorbate, zinc L-arginate, zinc L-arginine ascorbate and bis-ascorbate, zinc L-carnitate, zinc
5 L-carnitine ascorbate and bis-ascorbate, zinc phosphate, zinc acetate, zinc ascorbate, and zinc
6 bis-ascorbate.

1 **49.** A method in accordance with claim **36** in which said vanadium is in
2 the form of a member selected from the group consisting of vanadate, peroxovanadate,
3 vanadyl sulfate salts, and bis(maltolato)oxovanadium(IV).

1 **50.** A method in accordance with claims **30** or **32** in which said
2 D, α -tocopherol is present in the form of a member selected from the group consisting of
3 D, α -tocopherol succinate, D, α -tocopherol nicotinate, D, α -tocopherol picolinate,
4 D, α -tocopherol acetate, and tocotrienol.

1 **51.** A method in accordance with claims **40** or **50** in which said tocotrienol
2 is present in the form of a member selected from the group consisting of tocotrienol
3 succinate, tocotrienol nicotinate, tocotrienol picolinate, and tocotrienol acetate.

1 **52.** A method in accordance with claim **36** in which said chromium is in
2 the form of a member selected from the group consisting of chromium dinicotinate, and
3 chromium tripicolinate.

1 **53.** A method for treating a patient who is undergoing sulfonylurea therapy
2 for the prevention, management, and clinical amelioration of insulin resistance and type 2
3 diabetes and conditions giving rise thereto, to reduce undesirable physiological side effects,
4 and enhance the therapeutic effectiveness, of said sulfonylurea therapy, said method
5 comprising administering to said patient a unit dosage form comprising as active ingredients:

- 6 (a) L-carnitine,
- 7 (b) Ascorbic acid,
- 8 (c) Choline,

- 9 (e) Taurine,
- 10 (f) Folic Acid, and
- 11 (g) Magnesium.

1 54. A method in accordance with claim 53 in which said active ingredients
2 are formulated as a substantially homogeneous tablet or capsule that releases all of said active
3 ingredients into the stomach upon ingestion for contact with gastric fluid.

1 55. A method in accordance with claim 54 in which:

- 2 (a) said L-carnitine is in an amount ranging from about 90 mg to about 2500
- 3 mg, and
- 4 (b) said ascorbic acid is in an amount ranging from about 75 mg to about
- 5 3000 mg,
- 6 (c) said choline is in an amount ranging from about 15 mg to about 250 mg,
- 7 (d) said taurine is in an amount ranging from about 75 mg to about 3000 mg,
- 8 (e) said magnesium is in an amount ranging from about 30 mg to about 1000
- 9 mg, and
- 10 (d) said folic acid is in an amount ranging from about 0.03 mg to about 2 mg.

1 56. A method for treating a patient who is undergoing sulfonylurea therapy
2 for the preservation of plasma and mitochondrial membrane integrity for the prevention,
3 management, and clinical amelioration of insulin resistance and type 2 diabetes and
4 conditions giving rise thereto, to reduce undesirable physiological side effects, and enhance
5 the therapeutic effectiveness, of said sulfonylurea therapy, said method comprising
6 administering to said patient a unit dosage form comprising as active ingredients:

- 7 (a) D, α -lipoic acid,
- 8 (b) N, acetyl-cysteine,
- 9 (c) ubiquinone,
- 10 (d) selenium,
- 11 (e) a member selected from the group consisting of D, α -tocopherol and
- 12 tocotrienol,
- 13 (f) L-arginine, and
- 14 (g) tetrahydrobiopterin.

1 **57.** A method in accordance with claim **56** in which said active ingredients
2 are formulated as a substantially homogeneous tablet or capsule that releases all of said active
3 ingredients into the stomach upon ingestion for contact with gastric fluid.

1 **58.** A method in accordance with claim **57** in which:
2 (a) said D, α -lipoic acid is in an amount ranging from about 30 mg to about
3 1500 mg,
4 (b) said N, acetyl-cysteine is in an amount ranging from about 75 mg to
5 about 3900 mg,
6 (c) said ubiquinone is in an amount ranging from about 4.5 mg to about 225
7 mg,
8 (d) said selenium is in an amount ranging from about 0.02 mg to about 0.75
9 mg,
10 (e) said D, α -tocopherol or tocotrienol is in an amount ranging from about 15
11 mg to about 1600 mg,
12 (f) said L-arginine is in an amount ranging from about 75 mg to about 3100
13 mg, and
14 (f) said tetrahydrobiopterin is in an amount ranging from about 24 mg to about
15 3000 mg.

1 **59.** A method for treating a patient who is undergoing nocturnal
2 sulfonylurea therapy for the preservation of plasma and mitochondrial membrane integrity for
3 the prevention, management, and clinical amelioration of insulin resistance and type 2
4 diabetes and conditions giving rise thereto, to reduce undesirable physiological side effects,
5 and enhance the therapeutic effectiveness, of said sulfonylurea therapy, said method
6 comprising administering to said patient a unit dosage form comprising as active ingredients:
7 (a) melatonin,
8 (b) L-Carnitine,
9 (c) ubiquinone,
10 (d) folic acid,
11 (e) magnesium, and
12 (f) L-arginine.

1 **60.** A method in accordance with claim **59** in which said active ingredients
2 are formulated as a substantially homogeneous tablet or capsule that releases all of said active
3 ingredients into the stomach upon ingestion for contact with gastric fluid.

1 **61.** A method in accordance with claim **60** in which:
2 (a) said melatonin is in an amount ranging from about 0.15 mg to about 7.5
3 mg,
4 (b) said L-carnitine is in an amount ranging from about 90 mg to about 2500
5 mg,
6 (c) said ubiquinone is in an amount ranging from about 4.5 mg to about 225
7 mg,
8 (d) said folic acid is in an amount ranging from about 0.03 mg to about 2 mg,
9 (e) said magnesium is in an amount ranging from about 30 mg to about 1000
10 mg, and
11 (f) said L-arginine is in an amount ranging from about 75 mg to about 3100
12 mg.

1 **62.** A method for treating a patient who is undergoing sulfonylurea therapy
2 as an alternative to insulin for the prevention, management, and clinical amelioration of
3 insulin resistance and type 2 diabetes and conditions giving rise thereto, to reduce undesirable
4 physiological side effects, and enhance the therapeutic effectiveness, of said sulfonylurea
5 therapy, said method comprising administering to said patient a unit dosage form comprising
6 as active ingredients:

7 (a) vanadium,
8 (b) L-arginine,
9 (c) chromium, and
10 (d) zinc.

1 **63.** A method in accordance with claim **62** in which said active ingredients
2 are formulated as a substantially homogeneous tablet or capsule that releases all of said active
3 ingredients into the stomach upon ingestion for contact with gastric fluid.

1 **64.** A method in accordance with claim **63** in which:
2 (a) said vanadium is in an amount ranging from about 7.5 mg to about 375
3 mg,

(b) said L-arginine is in an amount ranging from about 75 mg to about 3100 mg,

(c) said chromium is in an amount ranging from about 0.01 mg to about 0.63 mg, and

(d) said zinc is in an amount ranging from about 1.5 mg to about 100 mg.

65. A method in accordance with claim 53 in which said unit dosage form is a bilayer tablet comprising an immediate-release layer and a sustained-release layer, said active ingredients are distributed between said immediate-release layer and said sustained-release layer in the following approximate proportions expressed as relative weight percents:

	<u>Immediate-Release Layer</u>	<u>Sustained-Release Layer</u>
L, carnitine	40-60%	balance
ascorbic acid	40-60%	balance
choline	100%	
folic acid	100%	
taurine	40-60%	balance
magnesium	40-60%	balance

66. A method in accordance with claim 56 in which said unit dosage form is a bilayer tablet comprising an immediate-release layer and a sustained-release layer, said active ingredients are distributed between said immediate-release layer and said sustained-release layer in the following approximate proportions expressed as relative weight percents:

	<u>Immediate-Release Layer</u>	<u>Sustained-Release Layer</u>
D,α-lipoic acid	40-60%	balance
N-acetyl-cysteine	40-60%	balance
ubiquinone	40-60%	balance
selenium	40-60%	balance
tocotrienol	100%	
L-arginine	40%-60%	balance
tetrahydrobiopterin	40%-60%	balance

67. A method in accordance with claim 59 in which said unit dosage form is a bilayer tablet comprising an immediate-release layer and a sustained-release layer, said active ingredients are distributed between said immediate-release layer and said sustained-release layer in the following approximate proportions expressed as relative weight percents:

		<u>Immediate-Release Layer</u>	<u>Sustained-Release Layer</u>
5			
6	melatonin	40-60 %	balance
7	L-carnitine	40-60%	balance
8	zinc	40%-60%	balance
9	folic acid	100%	
10	magnesium	40-60%	balance
11	ubiquinone	100%	

1 68. A method in accordance with claim 62 in which said unit dosage form
2 is a bilayer tablet comprising an immediate-release layer and a sustained-release layer, said
3 active ingredients are distributed between said immediate-release layer and said sustained-
4 release layer in the following approximate proportions expressed as relative weight percents:

		<u>Immediate-Release Layer</u>	<u>Sustained-Release Layer</u>
5			
6	vanadium	40-60 %	balance
7	L-arginine	40-60%	balance
8	chromium	40%-60%	balance
9	zinc	40%-60%	balance

1 69. A method in accordance with claim 56 in which said α -lipoic acid is in
2 the form of a member selected from the group consisting of an α -lipoic acid salt of a metal
3 ion selected from the group consisting of Mg^{2+} and Zn^{2+} , and a complex of α -lipoic acid, a
4 metal ion selected from the group consisting of Mg^{2+} and Zn^{2+} , and an anion selected from
5 the group consisting of hydroxide, halide, acetate, and ascorbate.

1 70. A method in accordance with claims 56, 59, or 62 in which said L-
2 arginine is in the form of a member selected from the group consisting of L-arginine
3 ascorbate, bis-L-arginine ascorbate, L-arginine salt of a metal ion selected from the group
4 consisting of Mg^{2+} and Zn^{2+} , bis-L-arginine salt of a metal ion selected from the group
5 consisting of Mg^{2+} and Zn^{2+} , and a complex of L-arginine or bis-L-arginine, a metal ion
6 selected from the group consisting of Mg^{2+} and Zn^{2+} , and an anion selected from the group
7 consisting of hydroxide, halide, acetate, and ascorbate.

1 71. A method in accordance with claims 53 or 59 in which said L-carnitine
2 is in the form of a member selected from the group consisting of L-carnitine ascorbate, bis-
3 L-carnitine ascorbate, L-carnitine salt of a metal ion selected from the group consisting of

4 Mg^{2+} and Zn^{2+} , bis-L-carnitine salt of a metal ion selected from the group consisting of Mg^{2+}
5 and Zn^{2+} , and a complex of L-carnitine or bis-L-carnitine, a metal ion selected from the group
6 consisting of Mg^{2+} and Zn^{2+} , and an anion selected from the group consisting of hydroxide,
7 halide, acetate, and ascorbate.

1 72. A method in accordance with claim 53 in which said L-aurine is in the
2 form of a member selected from the group consisting of L-aurine ascorbate, bis-L-aurine
3 ascorbate, L-aurine salt of a metal ion selected from the group consisting of Mg^{2+} and Zn^{2+} ,
4 bis-L-aurine salt of a metal ion selected from the group consisting of Mg^{2+} and Zn^{2+} , and a
5 complex of L-aurine or bis-L-aurine, a metal ion selected from the group consisting of Mg^{2+}
6 and Zn^{2+} , and an anion selected from the group consisting of hydroxide, halide, acetate, and
7 ascorbate.

1 73. A method in accordance with claims 53 or 59 in which said
2 magnesium is in the form of a member selected from the group consisting of magnesium,
3 magnesium L-arginate, magnesium L-arginine ascorbate and bis-ascorbate, magnesium α -
4 lipoate, magnesium α -lipoate ascorbate and bis-ascorbate, magnesium taurate, magnesium
5 taurine ascorbate and bis-ascorbate, magnesium L-acetylcysteine, magnesium L-carnitine,
6 magnesium L-carnitine ascorbate and bis-ascorbate, magnesium ascorbate and magnesium
7 bis-ascorbate.

1 74. A method in accordance with claim 62 in which said zinc is in the form
2 of a member selected from the group consisting of zinc halide, zinc sulfate, zinc L-carnitine,
3 zinc L-carnitine ascorbate and bis-ascorbate, zinc taurate, zinc taurine ascorbate and bis-
4 ascorbate, zinc L-arginate, zinc L-arginine ascorbate and bis-ascorbate, zinc L-carnitine, zinc
5 L-carnitine ascorbate and bis-ascorbate, zinc phosphate, zinc acetate, zinc ascorbate, and zinc
6 bis-ascorbate.

1 75. A method in accordance with claim 62 in which said vanadium is in
2 the form of a member selected from the group consisting of vanadate, peroxovanadate,
3 vanadyl sulfate salts, and bis(maltolato)oxovanadium(IV).

1 76. A method in accordance with claims 56 or 58 in which said
2 D, α -tocopherol is present in the form of a member selected from the group consisting of
3 D, α -tocopherol succinate, D, α -tocopherol nicotinate, D, α -tocopherol picolinate,
4 D, α -tocopherol acetate, and tocotrienol.

1 **77.** A method in accordance with claims **66** or **76** in which said tocotrienol
2 is present in the form of a member selected from the group consisting of tocotrienol
3 succinate, tocotrienol nicotinate, tocotrienol picolinate, and tocotrienol acetate.

1 **78.** A method in accordance with claim **36** in which said chromium is in
2 the form of a member selected from the group consisting of chromium dinicotinate, and
3 chromium tripicolinate.

1 **79.** A method for treating a patient who is undergoing combined biguanide
2 and combined biguanide and sulfonylurea therapy for the prevention, management, and
3 clinical amelioration of insulin resistance and type 2 diabetes and conditions giving rise
4 thereto, to reduce undesirable physiological side effects, and enhance the therapeutic
5 effectiveness, of said combined biguanide and sulfonylurea therapy, said method comprising
6 administering to said patient a unit dosage form comprising as active ingredients:

- 7 (a) L-carnitine,
- 8 (b) ascorbic acid,
- 9 (c) choline,
- 10 (e) taurine,
- 11 (f) folic acid, and
- 12 (g) magnesium.

1 **80.** A method in accordance with claim **79** in which said active ingredients
2 are formulated as a substantially homogeneous tablet or capsule that releases all of said active
3 ingredients into the stomach upon ingestion for contact with gastric fluid.

1 **81.** A method in accordance with claim **80** in which:

- 2 (a) said L-carnitine is in an amount ranging from about 90 mg to about 2500
3 mg, and
- 4 (b) said ascorbic acid is in an amount ranging from about 75 mg to about
5 3000 mg,
- 6 (c) said choline is in an amount ranging from about 15 mg to about 250 mg,
- 7 (d) said taurine is in an amount ranging from about 75 mg to about 3000 mg,
- 8 (e) said magnesium is in an amount ranging from about 30 mg to about 1000
9 mg, and
- 10 (d) said folic acid is in an amount ranging from about 0.03 mg to about 2 mg.

1 **82.** A method for treating a patient who is undergoing combined biguanide
2 and sulfonylurea therapy for the preservation of plasma and mitochondrial membrane
3 integrity for the prevention, management, and clinical amelioration of insulin resistance and
4 type 2 diabetes and conditions giving rise thereto, to reduce undesirable physiological side
5 effects, and enhance the therapeutic effectiveness, of said combined biguanide and
6 sulfonylurea therapy, said method comprising administering to said patient a unit dosage
7 form comprising as active ingredients:

- 8 (a) D, α -lipoic acid,
- 9 (b) N, acetyl-cysteine,
- 10 (c) ubiquinone,
- 11 (d) selenium,
- 12 (e) a member selected from the group consisting of D, α -tocopherol and
13 tocotrienol,
- 14 (f) L-arginine, and
- 15 (g) tetrahydrobiopterin.

1 **83.** A method in accordance with claim **82** in which said active ingredients
2 are formulated as a substantially homogeneous tablet or capsule that releases all of said active
3 ingredients into the stomach upon ingestion for contact with gastric fluid.

1 **84.** A method in accordance with claim **83** in which:

- 2 (a) said D, α -lipoic acid is in an amount ranging from about 30 mg to about
3 1500 mg,
- 4 (b) said N, acetyl-cysteine is in an amount ranging from about 75 mg to
5 about 3900 mg,
- 6 (c) said ubiquinone is in an amount ranging from about 4.5 mg to about 225
7 mg,
- 8 (d) said selenium is in an amount ranging from about 0.02 mg to about 0.75
9 mg,
- 10 (e) said D, α -tocopherol or tocotrienol is in an amount ranging from about 15
11 mg to about 1600 mg,
- 12 (f) said L-arginine is in an amount ranging from about 75 mg to about 3100
13 mg, and

14 (f) said tetrahydrobiopterin is in an amount ranging from about 24 mg to about
15 3000 mg.

1 85. A method for treating a patient who is undergoing nocturnal combined
2 biguanide and sulfonylurea therapy for the preservation of plasma and mitochondrial
3 membrane integrity for the prevention, management, and clinical amelioration of insulin
4 resistance and type 2 diabetes and conditions giving rise thereto, to reduce undesirable
5 physiological side effects, and enhance the therapeutic effectiveness, of said combined
6 biguanide and sulfonylurea therapy, said method comprising administering to said patient a
7 unit dosage form comprising as active ingredients:

- 8 (a) melatonin,
- 9 (b) L-Carnitine,
- 10 (c) ubiquinone,
- 11 (d) folic acid,
- 12 (e) magnesium, and
- 13 (f) L-arginine.

1 86. A method in accordance with claim 85 in which said active ingredients
2 are formulated as a substantially homogeneous tablet or capsule that releases all of said active
3 ingredients into the stomach upon ingestion for contact with gastric fluid.

1 87. A method in accordance with claim 86 in which:
2 (a) said melatonin is in an amount ranging from about 0.15 mg to about 7.5
3 mg,
4 (b) said L-carnitine is in an amount ranging from about 90 mg to about 2500
5 mg,
6 (c) said ubiquinone is in an amount ranging from about 4.5 mg to about 225
7 mg,
8 (d) said folic acid is in an amount ranging from about 0.03 mg to about 2 mg,
9 (e) said magnesium is in an amount ranging from about 30 mg to about 1000
10 mg, and
11 (f) said L-arginine is in an amount ranging from about 75 mg to about 3100
12 mg.

1 **88.** A method for treating a patient who is undergoing combined biguanide
2 and sulfonylurea therapy as an alternative to insulin for the prevention, management, and
3 clinical amelioration of insulin resistance and type 2 diabetes and conditions giving rise
4 thereto, to reduce undesirable physiological side effects, and enhance the therapeutic
5 effectiveness, of said combined biguanide and sulfonylurea therapy, said method comprising
6 administering to said patient a unit dosage form comprising as active ingredients:

- 7 (a) vanadium,
8 (b) L-arginine,
9 (c) chromium, and
10 (d) zinc.

1 **89.** A method in accordance with claim 88 in which said active ingredients
2 are formulated as a substantially homogeneous tablet or capsule that releases all of said active
3 ingredients into the stomach upon ingestion for contact with gastric fluid.

1 **90.** A method in accordance with claim 89 in which:

- 2 (a) said vanadium is in an amount ranging from about 7.5 mg to about 375
3 mg,
4 (b) said L-arginine is in an amount ranging from about 75 mg to about 3100
5 mg,
6 (c) said chromium is in an amount ranging from about 0.01 mg to about 0.63
7 mg, and
8 (d) said zinc is in an amount ranging from about 1.5 mg to about 100 mg.

1 **91.** A method in accordance with claim 89 in which said unit dosage form
2 is a bilayer tablet comprising an immediate-release layer and a sustained-release layer, said
3 active ingredients are distributed between said immediate-release layer and said sustained-
4 release layer in the following approximate proportions expressed as relative weight percents:

	<u>Immediate-Release Layer</u>	<u>Sustained-Release Layer</u>
L, carnitine	40-60%	balance
ascorbic acid	40-60%	balance
choline	100%	
folic acid	100%	
taurine	40-60%	balance

11 magnesium 40-60% balance

1 92. A method in accordance with claim 82 in which said unit dosage form
2 is a bilayer tablet comprising an immediate-release layer and a sustained-release layer, said
3 active ingredients are distributed between said immediate-release layer and said sustained-
4 release layer in the following approximate proportions expressed as relative weight percents:

	<u>Immediate-Release Layer</u>	<u>Sustained-Release Layer</u>	
5			
6	D,α-lipoic acid	40-60%	balance
7	N-acetyl-cysteine	40-60%	balance
8	ubiquinone	40-60%	balance
9	selenium	40-60%	balance
10	tocotrienol	100%	
11	L-arginine	40%-60%	balance
12	tetrahydrobiopterin	40%-60%	balance

1 93. A method in accordance with claim 85 in which said unit dosage form
2 is a bilayer tablet comprising an immediate-release layer and a sustained-release layer, said
3 active ingredients are distributed between said immediate-release layer and said sustained-
4 release layer in the following approximate proportions expressed as relative weight percents:

	<u>Immediate-Release Layer</u>	<u>Sustained-Release Layer</u>	
5			
6	melatonin	40-60 %	balance
7	L-carnitine	40-60%	balance
8	zinc	40%-60%	balance
9	folic acid	100%	
10	magnesium	40-60%	balance
11	ubiquinone	100%	

1 94. A method in accordance with claim 88 in which said unit dosage form
2 is a bilayer tablet comprising an immediate-release layer and a sustained-release layer, said
3 active ingredients are distributed between said immediate-release layer and said sustained-
4 release layer in the following approximate proportions expressed as relative weight percents:

	<u>Immediate-Release Layer</u>	<u>Sustained-Release Layer</u>	
5			
6	vanadium	40-60 %	balance
7	L-arginine	40-60%	balance
8	chromium	40%-60%	balance

9 zinc 40%-60% balance

1 **95.** A method in accordance with claim **92** in which said α -lipoic acid is in
2 the form of a member selected from the group consisting of an α -lipoic acid salt of a metal
3 ion selected from the group consisting of Mg^{2+} and Zn^{2+} , and a complex of α -lipoic acid, a
4 metal ion selected from the group consisting of Mg^{2+} and Zn^{2+} , and an anion selected from
5 the group consisting of hydroxide, halide, acetate, and ascorbate.

1 **96.** A method in accordance with claims **82**, **85**, or **88** in which said L-
2 arginine is in the form of a member selected from the group consisting of L-arginine
3 ascorbate, bis-L-arginine ascorbate, L-arginine salt of a metal ion selected from the group
4 consisting of Mg^{2+} and Zn^{2+} , bis-L-arginine salt of a metal ion selected from the group
5 consisting of Mg^{2+} and Zn^{2+} , and a complex of L-arginine or bis-L-arginine, a metal ion
6 selected from the group consisting of Mg^{2+} and Zn^{2+} , and an anion selected from the group
7 consisting of hydroxide, halide, acetate, and ascorbate.

1 **97.** A method in accordance with claims **78** or **85** in which said L-carnitine
2 is in the form of a member selected from the group consisting of L-carnitine ascorbate, bis-
3 L-carnitine ascorbate, L-carnitine salt of a metal ion selected from the group consisting of
4 Mg^{2+} and Zn^{2+} , bis-L-carnitine salt of a metal ion selected from the group consisting of Mg^{2+}
5 and Zn^{2+} , and a complex of L-carnitine or bis-L-carnitine, a metal ion selected from the group
6 consisting of Mg^{2+} and Zn^{2+} , and an anion selected from the group consisting of hydroxide,
7 halide, acetate, and ascorbate.

1 **98.** A method in accordance with claim **78** in which said L-taurine is in the
2 form of a member selected from the group consisting of L-taurine ascorbate, bis-L-taurine
3 ascorbate, L-taurine salt of a metal ion selected from the group consisting of Mg^{2+} and Zn^{2+} ,
4 bis-L-taurine salt of a metal ion selected from the group consisting of Mg^{2+} and Zn^{2+} , and a
5 complex of L-taurine or bis-L-taurine, a metal ion selected from the group consisting of Mg^{2+}
6 and Zn^{2+} , and an anion selected from the group consisting of hydroxide, halide, acetate, and
7 ascorbate.

1 **99.** A method in accordance with claims **79** or **85** in which said
2 magnesium is in the form of a member selected from the group consisting of magnesium,
3 magnesium L-arginate, magnesium L-arginine ascorbate and bis-ascorbate, magnesium α -
4 lipoate, magnesium α -lipoate ascorbate and bis-ascorbate, magnesium taurate, magnesium

5 taurine ascorbate and bis-ascorbate, magnesium L-acetylcysteine, magnesium L-carnitine,
6 magnesium L-carnitine ascorbate and bis-ascorbate, magnesium ascorbate and magnesium
7 bis-ascorbate.

1 **100.** A method in accordance with claim **88** in which said zinc is in the form
2 of a member selected from the group consisting of zinc halide, zinc sulfate, zinc L-carnitine,
3 zinc L-carnitine ascorbate and bis-ascorbate, zinc taurate, zinc taurine ascorbate and bis-
4 ascorbate, zinc L-arginate, zinc L-arginine ascorbate and bis-ascorbate, zinc L-carnitine, zinc
5 L-carnitine ascorbate and bis-ascorbate, zinc phosphate, zinc acetate, zinc ascorbate, and zinc
6 bis-ascorbate.

1 **101.** A method in accordance with claim **88** in which said vanadium is in
2 the form of a member selected from the group consisting of vanadate, peroxovanadate,
3 vanadyl sulfate salts, and bis(maltolato)oxovanadium(IV).

1 **102.** A method in accordance with claims **82** or **84** in which said
2 D, α -tocopherol is present in the form of a member selected from the group consisting of
3 D, α -tocopherol succinate, D, α -tocopherol nicotinate, D, α -tocopherol picolinate,
4 D, α -tocopherol acetate, and tocotrienol.

1 **103.** A method in accordance with claims **92** or **102** in which said
2 tocotrienol is present in the form of a member selected from the group consisting of
3 tocotrienol succinate, tocotrienol nicotinate, tocotrienol picolinate, and tocotrienol acetate.

1 **104.** A method in accordance with claim **88** in which said chromium is in
2 the form of a member selected from the group consisting of chromium dinicotinate, and
3 chromium tripicolinate.